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STUDIES IN WATER METABOLISM OF THE
CAT. THE INFLUENCE OF DEHYDRATION
ON BLOOD CONCENTRATION, THERMO-
REGULATION, RESPIRATORY EXCHANGE,
AND METABOLIC-WATER PRODUCTION

A DISSERTATION SUBMITTED TO THE
GRADUATE FACULTY IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF ZOÖLOGY

By
GEORGE THORNHILL CALDWELL

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TION¹

(Five figures)

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INTRODUCTION

THE author (1925) showed that, in a number of poikilothermic animals representing several phyla and xeric, mesic, and hydric habitats, dehydration resulted in an increased carbon-dioxide production. This suggested that, in animals which exist under arid conditions, where water is one of the principal factors in survival, a decrease in water content of the body might lead to a greater production of water of oxidation through increased respiratory exchange.

Before the effects of dehydration could be studied in the homotherms, it became necessary to know whether the existence of a connection between the metabolism of water and the homothermal mechanism, as proposed by Balcar, Sansum, and Woodyatt (1919), Barbour and Tolstoi (1922), and Rogers (1924*b*), would manifest itself by an increase in body temperature when the animals were dehydrated by water deprivation in a manner somewhat simulating desert conditions. Balcar, Sansum, and Woodyatt (1919) dehydrated dogs by intravenous injections of diuretic agents, glucose, lactose, and sodium-chloride solutions, and reported an increase in body temperature of 11°-23.6° F. Keith (1924) repeated the experiments and found that with smaller dosage but a higher ratio of water output there was no increase in body temperature if the loss of water did not exceed 10 per cent of the body weight. With greater losses the maximum increase in body temperature was less than 4° F., and

¹ The author takes pleasure in his acknowledgment of the helpful suggestions and criticisms of Dr. W. C. Allee, under whose supervision this work has been accomplished.

in many experiments less than 1° F. Barbour and Tolstoi (1922) exposed dogs to hot and cold baths and observed respectively concentration and dilution of the blood. These responses could not be elicited in the absence of the heat-regulating mechanism, brought about by the transection of the cord at the sixth cervical level.

Since the work reported in this paper has been in progress, dehydration experiments with sugar and salt solutions have been repeated by many workers with conflicting results. Keith and Whalen (1926) reported that marked hyperpyrexia did not occur when all possible toxic factors connected with preparation and administration of the sugar solutions were excluded. Andrews (1926) showed that if a dog was allowed to ventilate his tongue freely he could regulate his body temperature "fairly well" in extreme dehydration from intravenous injections of sugar and salt solutions; while, if its mouth was tied shut, there was a rise of 1° - 2° F. with moderate dehydration and in extreme dehydration a terminal rise of 10° - 12° F. This conclusion is substantiated by the fact that dogs depend on the upper respiratory tract mainly for water evaporation and by the statement of Roundtree (1922) that the rectal temperature of tracheotomized dogs rose from 39° to 42° and 44° C. when they were placed in the sunshine. This source of error seems to have been overlooked by other workers, and may have been responsible for conflicting reports on the effects of sugar diuresis on body temperature.

The literature on water metabolism is very extensive and has been reviewed in part by Roundtree (1922) in relation to water balance, by Marriott (1923) in relation to blood changes observed by pediatricians in the acute anhydremia of infants, by Schiff (1929) in relation to infant toxicosis following water losses; and recently some of the literature relative to water balance has been reviewed by Adolph (1930). Underhill and co-workers (1923) reported blood concentration changes in extensive superficial burns.

Animal experimentation on the general physiological effects of dehydration has been rather limited and with little uniformity in conditions. Czerny (1894) deprived young cats of food and water and studied body-temperature and blood-concentration effects when the animals were kept in dry air at temperatures from 31° to 39.5° C. Straub (1899) deprived young dogs of water for three days and re-

reported on metabolism and circulation determinations. Adolph (1921) studied the effects of water loss in man over short periods of time. Underhill and Kapsinow (1922) reported on blood concentration in fasting rabbits deprived of water, and Underhill and Roth (1922) found an increase in hemoglobin in fasting dogs deprived of water. Keith (1922) reported a decrease in blood volume of dogs when food and water were withheld. Korth and Marx (1928) found fluctuations in hemoglobin in the blood of dogs during thirst.

The original purpose of these experiments was to determine the effects of disturbance of the water balance on the ability of the animal to regulate body temperature. The limited knowledge available on the effects of dehydration, as pointed out by Roundtree (1922) and more recently by Gamble (1929) and Schiff (1929), seemed to justify the extension of the problem to include blood counts as an indication of the extent of anhydremia caused by extreme dehydration, to attempt the estimation of metabolic water production, and to determine the effect of dehydration on the respiratory exchange.

It should be emphasized that, unlike the majority of experiments reported on dehydration effects, the animals in these experiments were fed regularly. Starvation undoubtedly modified the results in some cases near the end of the experiments, but usually the latter were stopped soon after the animal refused food on account of the mechanical difficulties encountered in deglutition from reduced salivary secretion. This does not necessarily mean that the animals ate sufficient food to supply the total energy output, and without doubt the effects of dehydration are obscured at times by starvation.

A method has been devised which produced not so rapid but just as severe dehydration, without toxic etiologic factors which might accompany intravenous injections of hypertonic solutions, which permitted of determinations of water losses by evaporation as well as through other sources and which provided for air-sampling for gas analyses. These features have not been incorporated generally in other methods.

EXPERIMENTAL PROCEDURE

The dehydration apparatus (Fig. 1) consisted of a 22-liter bell jar with ground flange, which rested on plate glass and served as the

animal chamber. Two porcelain pans of a diameter slightly less than that of the bell jar were fitted into one another. The bottom of the inner pan was perforated and supplied with feet which rested on the inner bottom of the outer pan. These were placed in the animal chamber and prevented the cat from consuming any appreciable quantity of its urine. The neck of the jar was provided with an inlet and outlet tube, a glass tube with stopcock through which samples

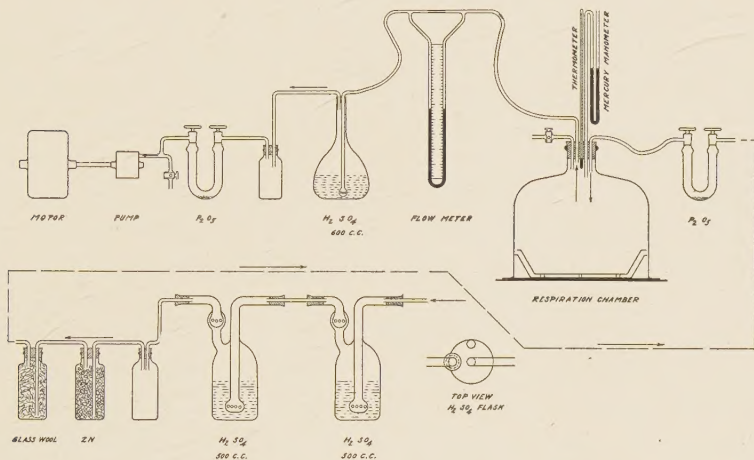


FIG. 1.—Apparatus used in dehydration of cats and collection of water vapor from respiration and evaporation from excreta. Bottles not labeled are traps. The apparatus was connected with an outdoor air intake.

of air could be drawn, a thermometer, and a mercury manometer which facilitated tests for leaks in the system. Outdoor air was drawn through two 1-quart William's gas-washing bottles containing 500 cc. of concentrated H_2SO_4 c.p., through an empty bottle which served as a trap, another bottle containing granulated zinc, a third bottle filled with glass wool, and then into an absorption tube containing P_2O_5 . The air then passed through a flowmeter and into the animal chamber. From the animal chamber the air was drawn into a 1-liter volumetric flask which contained 600 cc. of H_2SO_4 . This flask was fitted with a glass intake tube through which the air passed into the acid through fine holes which broke up the air bubbles so that it was not necessary to use two H_2SO_4 ab-

sorption flasks to absorb the water of respiration and evaporation. This absorption flask was connected by glass tubing, without rubber, to a small empty bottle for a trap, which was always weighed with the flask. At this point another absorption tube containing P_2O_5 was inserted in the system. When the P_2O_5 showed the presence of moisture, the acid in the absorption flask was renewed. The same method was used for the William's gas-washing bottles. From the P_2O_5 tube the air passed into the pump, which was driven by an electric motor. A valve near the pump made it possible to keep the flow of air through the animal chamber constant. As the quantity of acid in the flask increased due to water absorption, the resistance in the system increased and the air flow decreased. This was overcome by the selection of absorption tubes with small bore inlet and outlet apertures for the P_2O_5 . These provided a fixed resistance in the air line, which was always higher than the total resistance elsewhere in the system even with maximum dilution of the H_2SO_4 from water absorption. At intervals, air, at the usual rate of flow, was bubbled through methyl-orange solution to test for H_2SO_4 . These tests were consistently negative. The flowmeter was calibrated on a standard meter tester.¹ The apparatus could be quickly tested for leaks by the adjustment of the valve to create a considerable vacuum, followed by closure of the two ends of the system and subsequent observation of the mercury in the manometer of the animal chamber.

Body-temperature determinations were made by way of the rectum with a standard clinical thermometer. Blood counts were made with a standard haemocytometer. For red blood corpuscles, the blood was diluted 1-200 with Toisson's solution. One per cent acetic acid and a dilution of 1-20 were employed for white counts. Usually, 80 squares were counted for red corpuscles and 16 large squares for the white corpuscles.

Gas analyses were made in a Newcomer modification of the Haldane gas-analysis apparatus. The procedure described by Carpenter (1915) was followed throughout. Gas samples were drawn by means of a mercury pump directly from the animal chamber into gas-

¹ The author is indebted to the Tucson Gas, Electric Light and Power Company for the use of apparatus and assistance in the calibration of the flowmeters.

collecting tubes of 125 cc. capacity provided with stopcocks at either end. Ten cubic centimeters of acidulated water in the collecting tubes served to completely saturate the air with moisture before the sample was introduced into the gas-analysis apparatus. As the capacity of the burette of the Haldane was only 10 cc., a 75-cc. sample was sufficient for several analyses.

The experiments were conducted in Tucson, Arizona, upon full-grown cats acclimated to the semi-arid conditions of that region. Blood counts were made on many cats in the attempt to select healthy individuals. Before actual experimentation was begun, each of the experimental animals had been for some time under observation in the laboratory, on a diet of cooked, lean meat; they were accustomed to handling and to confinement. The experiments on 13 males and 3 females and the temperature control data on 6 cats have been included in this report. The females had been isolated sufficiently long to determine that they were not pregnant. Data have not been included from several experiments which were discontinued because of mechanical difficulties with apparatus or illness of the animal from diarrhea which, since it occurred early in the experiment, could be attributed to chance infection rather than a lowered resistance from dehydration.

For the experiments in which carbon-dioxide production and oxygen absorption were not determined, the procedure was the same throughout. Blood samples were taken, the rectal temperature recorded, the animal weighed, the desiccator for absorption of water from the animal chamber weighed, and the animal placed in the apparatus. The valve was adjusted to give the desired flow of air, and the animal was undisturbed until the next observations. At 12-hour intervals the animal was removed from the desiccator, weighed, rectal temperature recorded, and fed as much cooked, lean meat as it would eat. All visible fat was removed from the meat, which almost without exception was beef. A 10-gm. sample of the food was taken for determination of water content by drying to constant weight at a temperature of 100° C. The temperature of the animal chamber was recorded immediately before the animal was removed. The urine and feces were collected from pans and weighed. The water content of the feces was determined in the same manner as for

the food sample. The outlet desiccator was weighed and water losses from evaporation recorded. The weight of the food eaten was determined and the cat weighed to check any loss of excreta while it was out of the animal chamber and as a check against the weight of food consumed. At 72-hour intervals blood samples were taken and red and white corpuscle counts made. With the exception of cat No. 15, the animals received no water throughout the experiment except that from the cooked, lean meat; cat No. 15 received no free water but for 5 of the 16 days was fed uncooked, lean beef which contained a higher water content than the cooked meat.

In the experiments in which respiratory exchange was determined, the procedure was identical with the foregoing except that the animals were kept in the animal chamber for several days prior to the experimental period to accustom them to all the experimental conditions except dehydration. For this period, outdoor air with normal degree of humidity was passed through the animal chamber at the same rate as when the animal was to be desiccated. For this adaptation period, 2-4 days, gas analyses were made daily and the cats were fed lean, cooked meat and given water *ad libitum*. Usually, after 24 hours in the apparatus, the excitement from the close confinement had subsided and the rate of respiration was normal. These preliminary analyses furnished the data for comparison of normal and experimental carbon-dioxide production and oxygen consumption. For the duration of the experiment gas analyses of the air from the animal chamber were made at 72-hour intervals. Barometer readings were taken at the time of analysis. The gas samples were taken when the animal was at rest and from 10 to 12 hours, occasionally less, after the last meal.

GENERAL OBSERVATIONS

The cats apparently suffered more from thirst during the first 5 or 6 days of the experiment and, for this period, were more irritable than later. After this period there was a decided reduction in response to external stimuli, particularly noted when punctures were made to obtain blood samples. As dehydration progressed, the cats slept more and, when not asleep, exhibited marked somnolence. In some of the longer experiments there was almost a total absence

of response to skin stimuli at the close of the experiment. The skin became rough and loose, with marked reduction in turgor and increased hair loss. The feces were hard and dry. Diarrhea was observed in only one case. Kudo (1921a) observed a greater tendency toward diarrhea in his studies on the effect of thirst on weight of rats.

Opacity of the lens, extension of the penis, hemorrhage from the nose, and paralysis of the posterior extremity, all observed by Kudo, were not present in the cats. Congestion of the conjunctiva was observed in some cases, as found by Kudo in rats. In extreme dehydration there was a marked depression of the central nervous system, accompanied by aphonia and dysphagia. There seemed to be little tolerance of thirst.

EXTENT OF DEHYDRATION

The administration of diuretics and the intravenous injections of hypertonic solutions to reduce the water content of the body involve radical changes in the organs which have to do with the regulation of water balance. The experiments reported here were designed to diminish the water content of the animal gradually to afford the animal an opportunity to adjust its needs, so far as possible, to a diminution in total water content uncomplicated by the action of drugs or other foreign substances.

Unlike the majority of work on dehydration, a careful determination of all water leaving the body has been made, as well as all water received by the animal. The intake-output ratios given below (Table I) include water lost by respiration, by evaporation from the body surface, and from the excreta. It has not been possible to distinguish between water of respiration and other water losses, because evaporation from urine and feces, when present in the pans, added to the weight of the outlet desiccator.

While the intake-output ratios are important, the actual difference between the total water intake and output expressed in percentage of the original body weight, and designated as negative water balance, seems to offer a better basis for some comparisons. The daily output of urine at the expense of the body tissue is surprisingly high in severe dehydration (Table I). The low intake-output ratio for cat No. 15 was the result of the large quantity of un-

cooked meat which it ate for 5 of the 16 days of the experiment. This cat weighed only 1,225 gm. at the beginning of the experiment and gained in weight when fed uncooked, lean meat. This would indicate that carnivorous animals may live long periods without access to free water. Under the conditions of the experiment, from 12 to 17 days was the maximum limit of desiccation without death intervening. The quantity of food taken and variations in room temperature were important factors in the duration of desiccation. Hall (1922), under somewhat similar conditions, found that the house mouse withstood desiccation for 8–16 days, while the wood mouse and meadow mouse gave up water more quickly.

As one phase of the problem was a study of the ability of the animal to regulate body temperature with different degrees of dehydration, no attempt was made to keep the animal chamber at constant temperature. The greatest variation recorded in the temperature of the animal chamber for the duration of a given experiment was 7° C. One-half of the experiments had recorded temperature changes of less than 5° C. These variations were principally differences between morning and evening temperatures of the room.

Czerny (1894) found that young cats, 209–685 gm., died after 15 days without food and water when kept at a temperature of 31°–32.5° C.; after 8 days at a temperature of 33.1–35.0° C., and after 20 hours at a temperature of 38.8–39.5° C. Such temperatures are much higher than the animal-chamber temperatures recorded in these experiments. Rogers (1924*a*) showed that complete destruction of the thalamus in decerebrate pigeons is followed by excessive diuresis with estimated water loss at the rate of 10–60 per cent of fasting weight in 24 hours. With water loss at a rate greater than 18 per cent of body weight in 24 hours, the birds could not be kept alive for periods of more than 36 hours. Czerny (1894) observed that young cats at a temperature of 33°–35° C. lost 45.9 per cent of body weight, while young cats at 38.0°–39.0° C. died when the body weight loss averaged 24 per cent.

THERMOREGULATION DURING DEHYDRATION

Since the literature on heat regulation has been reviewed by Barbour (1921), only the papers having a significant relation to water

TABLE I
DAILY INTAKE AND OUTPUT OF WATER, WITH RATIOS AND NEGATIVE
BALANCE IN PERCENTAGE OF ORIGINAL BODY WEIGHT

DAYS	CAT No. 1		CAT No. 5		CAT No. 15		CAT No. 17	
	Intake	Output	Intake	Output	Intake	Output	Intake	Output
1.....	28.2	123.0	45.5	124.0	18.7	52.0	19.3	57.0
2.....	49.9	118.0	51.3	142.6	75.9	60.2	116.3	119.4
3.....	89.2	106.0	70.4	120.9	91.3	79.5	53.2	110.9
4.....	57.3	139.0	31.8	238.8	95.8	78.0	17.1	187.0
5.....	79.9	127.1	70.0	59.7	71.7	88.5	14.1	95.5
6.....	45.5	115.5	20.4	109.6	17.3	85.9	15.7	71.0
7.....	24.5	91.0	40.0	121.3	99.5	69.0	1.9	59.5
8.....	49.3	99.4	17.6	63.1	87.6	98.0		34.0*
9.....	15.3	110.5	26.5	78.2	24.7	80.8		
10.....	43.7	74.0	25.9	71.3	19.9	59.0		
11.....	118.4	94.7	38.5	73.4	60.4	51.0		
12.....	6.8	106.5	27.9	82.6	32.0	65.5		
13.....	9.4	69.0	22.7	53.4	24.1	57.0		
14.....		51.0*	11.3	113.9	28.0	44.0		
15.....					11.7	60.0		
16.....					4.3	42.8		
Totals.....	617.4	1,424.7	499.8	1,452.8	762.9	1,071.2	237.6	734.3
Ratios.....	1:2.30		1:2.90		1:1.40		1:3.09	
Negative balance...	28.4%		30.9%		25.1%		22.7%	

* = 12 hours only.

TABLE I—Continued

DAYS	CAT No. 20		CAT No. 22		CAT No. 23		CAT No. 30	
	Intake	Output	Intake	Output	Intake	Output	Intake	Output
1.....	0.0	49.5	21.8	49.5	29.0	71.0	50.8	92.0
2.....	30.1	33.5	30.9	138.0	24.0	72.0	84.0	110.9
3.....	12.5	59.0	26.4	113.4	25.0	93.5	95.0	117.0
4.....	19.9	209.0	54.9	99.5	12.4	82.1	67.4	106.0
5.....	27.2	64.0	48.6	131.5	19.4	55.5	57.6	107.5
6.....	22.2	82.9	26.1	142.0	13.3	58.5	83.8	105.8
7.....	30.6	30.0	41.6	111.5	8.9	46.5	53.6	105.0
8.....	18.7	131.5	21.4	93.5	17.2	47.0	11.8	103.2
9.....	15.2	66.0	26.4	71.0	25.5	29.7	20.9	100.4
10.....	61.7	73.5	0.6	76.0	26.2	59.1	13.0	65.4
11.....	20.5	46.5	6.1	32.0	3.3	62.5	22.8	58.8
12.....		54.0*	19.5	75.4			10.8	72.3
13.....			28.2	55.5				
14.....				31.0*				
Totals.....	258.6	899.4	352.5	1,219.8	204.2	677.4	571.5	1,144.3
Ratios.....	1:3.47		1:3.46		1:3.31		1:2.00	
Negative balance...	32.9%		26.3%		33.9%		20.9%	

* = 12 hours only.

TABLE I—*Continued*

DAYS	CAT No. 33		CAT No. 35		CAT No. 36		CAT No. 48	
	Intake	Output	Intake	Output	Intake	Output	Intake	Output
1.....	69.6	199.5	50.9	164.7	20.2	102.5	13.4	70.5
2.....	64.3	102.5	70.5	119.5	45.1	107.0	10.3	47.0
3.....	44.9	135.5	66.1	140.0	40.3	70.5	10.5	46.0
4.....	57.2	99.2	51.3	56.5	22.5	105.0	0.0	58.2
5.....	55.8	117.0	34.0	103.4	45.9	74.9	1.4	37.5
6.....	35.7	123.5	24.0	115.0	31.7	90.0	5.1	41.5
7.....	31.7	61.5	18.1	106.5	24.1	56.0	0.8	39.5
8.....	19.7	81.0	25.3	92.5	18.5	76.0	0.8	42.5
9.....	25.7	68.0	23.8	88.5	19.0	71.1		46.5
10.....	16.5	62.0	24.1	61.0	17.9	57.5		
11.....	14.8	63.5	20.1	67.5	16.2	74.0		
12.....	23.8	55.5	4.7	56.5	9.9	60.5		
13.....	16.6	59.5			11.7	61.5		
14.....	7.4	56.5			5.9	56.0		
15.....					3.0	44.0		
Totals.....	483.7	1,284.7	412.9	1,171.6	331.9	1,106.5	42.3	429.2
Ratios.....	1:2.65		1:2.83		1:3.33		1:10.1	
Negative balance...	24.2%		31.6%		28.3%		16.6%	

TABLE I—*Continued*

DAYS	CAT No. 50		CAT No. 54		CAT No. 56		CAT No. 58	
	Intake	Output	Intake	Output	Intake	Output	Intake	Output
1.....	12.1	38.5	38.0	70.5	8.9	108.2	22.2	77.0
2.....	28.9	93.5	50.0	149.0	10.6	68.0	18.5	81.5
3.....	29.2	64.7	15.6	106.6	1.7	66.4	8.6	64.0
4.....	15.9	79.5	24.1	76.5	0.0	53.5	3.3	45.5
5.....	21.0	63.5	30.7	76.0		46.3	0.3	60.7
6.....	28.6	86.0	16.9	87.6		42.0	0.9	43.5
7.....	23.4	74.0	10.9	64.0			0.0	40.0
8.....	16.4	63.0	0.0	67.9				48.0
9.....	12.5	57.0		42.5				45.0
10.....	16.0	54.5		49.4				
11.....	14.9	50.0		40.0				
12.....	6.4	67.4		38.5				
Totals.....	225.3	791.6	186.2	868.5	21.2	384.4	53.8	505.2
Ratios.....	1:3.51		1:4.66		1:18.1		1:9.39	
Negative balance...	29.0%		30.1%		20.2%		19.3%	

metabolism, and especially dehydration, will receive attention here.

Czerny (1894) reported an increase in body temperature of young cats deprived of water and food at temperatures of 33° – 39° C., but did not state extent of increase. Sonderstrom and DuBois (1917) found a diminished output of water in typhoid-fever patients. Meyer, Cohen, and Carlson (1918) produced fevers experimentally in dogs and recorded a diminution in gastric secretion. Balcar, Sansum, and Woodyatt (1919) produced body temperature increases of 11° – 23.6° F. in dogs dehydrated by intravenous injections of sugar and salts, and concluded that fever is due to a deficit of free water resulting from an abnormal tendency on the part of colloids to bind water. Barbour and Howard (1920) found a concentration of the blood in coli fever in dogs, and Barbour and Freedman (1920) found that salivary secretion following pilocarpine was much reduced in coli-fever dogs. Keith (1924) dehydrated dogs by intravenous injections of glucose and reported an increase in body temperature, but repeated the work later (Keith and Whalen, 1926) and found that there was no marked hyperthermia when toxic factors were eliminated.

Rogers (1924a) produced hyperthermia in decerebrate pigeons by complete destruction of the thalamus with electrocautery. Hyperthermia only occurred when there was a diuresis sufficient to produce anhydremia. Rogers suggested that the rate of water loss was more important in production of hyperthermia than the actual quantity lost. Kayser (1929) found that decerebrate pigeons with cauterized thalamus became polyuric and were not able to regulate temperature, but that when the diuresis ceased, the ability to regulate temperature reappeared immediately. Kayser also produced polyuria in rabbits by puncture of the fourth ventricle and recorded a hypothermia accompanied by a reduction of 14.2–27.6 per cent in respiratory exchanges and concluded that thermoregulation fails when hydration equilibrium is disturbed. Dragstedt and Ellis (1929) dehydrated dogs to depress the volume of gastric juice secreted, and reported normal body temperature throughout the dehydration periods. This brief and incomplete summary of the literature on the relation of thermoregulation and water metabolism seems to indi-

cate some connection other than the passive rôle of water in heat conservation and dissipation for which it is so admirably suited because of its peculiar physical properties.

The results of these experiments (Tables II and III) clearly show

TABLE II
AVERAGES OF MORNING AND EVENING TEMPERATURES OF DEHYDRATED
CATS AND CORRESPONDING TEMPERATURES OF THE RESPIRATION
CHAMBER IN DEGREES CENTIGRADE

DAYS	CAT NO. 1		CAT NO. 5		CAT NO. 15		CAT NO. 17		CAT NO. 20		CAT NO. 22	
	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber
1.....	38.8	21.0	39.3	24.7	38.6	22.0	38.5	27.5	38.6	24.7	38.6	22.5
2.....	38.3	22.1	38.8	24.7	38.3	22.7	38.5	27.3	38.4	25.7	38.7	24.0
3.....	38.1	22.5	38.6	24.2	38.7	21.7	38.3	25.5	38.3	25.7	38.2	24.2
4.....	38.3	22.5	38.5	23.2	39.1	23.8	38.3	26.0	38.5	26.3	38.7	25.3
5.....	38.1	22.5	38.4	24.0	38.7	24.0	38.2	26.2	38.4	26.0	38.6	24.5
6.....	37.5	20.0	38.6	25.0	38.5	25.2	38.3	25.7	38.4	24.7	39.3	25.7
7.....	37.6	23.5	38.2	24.5	38.4	26.0	38.3	24.5	38.6	21.5	38.7	23.6
8.....	38.3	24.0	38.2	25.5	38.9	24.0	38.3	25.5	38.7	23.3	38.4	24.5
9.....	38.3	23.5	38.1	24.7	38.8	23.0			38.7	24.0	38.6	25.8
10.....	38.3	24.0	38.1	24.2	38.6	23.5			38.6	25.3	38.5	26.0
11.....	38.2	23.0	38.0	23.5	38.5	21.7			38.7	23.0	38.4	22.2
12.....	38.3	24.0	38.4	24.5	38.6	24.2			38.6	24.3	38.4	25.0
13.....	38.3	24.3	38.6	24.5	38.3	23.5					38.1	20.2
14.....			38.4	25.0	38.3	25.5					38.5	21.8
15.....					38.3	24.8						
16.....					38.5	25.7						

TABLE II—Continued

DAYS	CAT NO. 23		CAT NO. 30		CAT NO. 33		CAT NO. 35		CAT NO. 36	
	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber
1.....	38.4	27.0	37.9	24.2	38.7	27.0	38.7	28.7	38.5	26.4
2.....	38.7	27.0	38.1	23.8	38.3	24.0	38.5	28.2	39.0	27.5
3.....	39.2	28.0	38.1	24.7	38.2	25.0	38.1	25.2	38.5	25.6
4.....	39.1	26.5	38.3	26.5	38.2	25.0	37.7	26.0	38.9	27.4
5.....	38.7	26.5	38.4	28.1	38.4	26.4	38.3	26.4	38.9	27.0
6.....	38.5	24.3	38.1	27.2	38.6	27.1	38.4	26.1	38.5	25.5
7.....	38.6	26.0	38.3	27.0	38.6	27.0	38.4	26.1	38.5	25.6
8.....	38.7	24.0	38.2	26.6	38.4	27.9	38.7	27.9	38.8	25.5
9.....	38.6	25.5	38.0	26.1	38.4	26.9	38.4	26.3	38.4	25.7
10.....	38.5	25.5	38.1	26.9	38.2	26.7	38.2	24.0	38.3	25.2
11.....	38.2	24.2	38.5	28.4	38.3	26.2	38.1	26.0	38.7	26.5
12.....			38.5	26.8	38.2	25.7	38.1	25.1	38.9	28.0
13.....					38.3	27.3			38.6	24.3
14.....					38.1	25.5			38.9	26.0
15.....									38.7	25.5

TABLE II—Continued

DAYS	CAT No. 48		CAT No. 50		CAT No. 54		CAT No. 56		CAT No. 58	
	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber	Cat	Chamber
I.	38.4	24.7	38.7	27.2	38.8	27.2	38.6	27.2	38.7	28.0
2.	38.4	23.5	38.8	26.7	38.8	26.0	38.5	26.7	38.3	27.7
3.	37.8	22.7	39.0	28.7	38.8	28.0	38.8	29.7	38.8	30.0
4.	38.1	24.0	38.8	27.5	38.9	29.0	38.9	30.0	39.1	30.5
5.	38.1	24.0	38.7	27.0	39.0	29.0	38.6	28.5	38.8	29.5
6.	38.3	24.2	38.8	27.7	39.0	30.5	38.6	28.5	38.7	28.5
7.	38.3	24.0	38.6	27.0	38.9	30.0			39.4	28.0
8.	38.2	25.5	38.3	25.2	38.6	27.5			38.8	29.0
9.	38.3	26.5	38.3	25.7	38.7	27.5			38.6	29.5
10.			38.6	26.5	38.9	29.5				
11.			38.5	27.0	38.9	30.0				
12.			38.1	25.7	38.6	28.7				

TABLE III

AVERAGES OF MORNING AND EVENING TEMPERATURES OF CONTROL
CATS AND CORRESPONDING ROOM TEMPERATURES
IN DEGREES CENTIGRADE

DAYS	CAT No. 55	CAT No. 57	CAT No. 59	CAT No. 61	CAT No. 63	ROOM TEMPER- ATURE	CAT No. 67	
							Cat	Room Temper- ature
I.	39.0	39.0	39.1	39.1	39.4	23.2	38.9	21.7
2.	38.5	38.5	38.8	39.2	39.4	21.5	38.4	20.5
3.	38.9	39.4	39.1	39.0	39.5	21.7	38.7	20.5
4.	38.5	38.7	38.9	38.3	39.0	21.5	38.7	17.0
5.	38.4	38.5	39.0	38.5	40.0	21.0	38.7	21.0
6.	38.9	39.2	38.9	38.9	39.0	21.5	38.6	22.0
7.	38.7	38.7	38.8	39.0	38.3	21.0	39.0	19.5
8.	38.9	38.6	38.7	39.3	38.4	23.0	38.7	21.0
9.	38.6	38.6	38.5	39.1	38.3	22.0	38.9	21.5
10.	38.2	38.2	38.4	38.5	38.6	22.0	39.0	19.5
11.	38.3	38.3	38.4	38.5	38.5	22.2	38.5	21.0
12.	38.6	38.6	38.9	38.6	38.9	22.5	38.6	22.2
13.	38.8	38.8	38.5	39.1	39.0	22.7	38.5	22.5
14.	38.2	38.1	39.2	39.1	38.6	22.0	38.5	21.5
15.	38.5	38.5	39.3	38.6	38.5	23.5		

that it is possible to reduce the water content of adult cats practically to the vital limit without disturbance of the thermoregulation mechanism. Within a range of approximately 10° C. of external temperature, it is certain that the body-temperature variations of the experimental animals did not exceed those of the control animals.

The average of morning and evening temperatures tends to obscure the diurnal variations but was necessary to reduce the bulk of data. Whether these animals could have regulated their body temperature, as well as normal cats, when exposed to extremes of external temperature remains to be determined.

BLOOD CONCENTRATION DURING DEHYDRATION

Any disturbance of water metabolism which results in a negative water balance is followed by a concentration of the blood solids. A sudden loss of water from the body results in a greater blood concentration than when the same amount of water is lost over a longer period of time. Adolph (1921) found a 15 per cent concentration of the blood in man with a 5 per cent loss of body weight when the subject was sweated for a short time in a hot bath, as compared to a 2 per cent blood concentration when the same amount of fluid was lost by sweating over a period of 3 hours. Keith (1924) reported concentrations of blood plasma of 24-44 per cent in dogs dehydrated rapidly by intravenous injections of sugar solutions. Skelton (1927) determined that in the cat the skin contained 20 per cent of the total water, the muscles 50 per cent, and the blood 7 per cent. When dehydration takes place slowly, the reserves are drawn upon to restore the blood to a normal condition and blood concentration more nearly represents the condition of dehydration throughout the entire body.

In mammals, a sufficient amount of water must be excreted to hold in solution urea, salts, and other waste products in proper dilution for secretion by the kidneys. Adolph (1922) has demonstrated that there is a maximum concentration of urea and sodium chloride which can be excreted by a given individual. Regardless of this constant demand upon the body for water to eliminate the end-products of metabolism and salts, it has been repeatedly demonstrated that the concentration of the blood may be greatly increased without loss of life. Czerny (1894) reported an increase of 44 per cent in the red corpuscles of young cats desiccated at a temperature of 33°-35° C. Underhill and Kapsinow (1922) reported an increase of 40 per cent in hemoglobin of fasting dogs deprived of water, and Underhill and co-workers (1923) found an increase in hemoglobin

of more than 100 per cent in man following extensive superficial burns. Schiff, Eliasberg, and Bayer (1924) reduced the water intake of young children for 3 days and reported an increase of 40 per cent in protein concentration of the blood; and Schiff (1929) reported a 38 per cent increase in blood proteins of young dogs fed milk powder.

A number of methods have been used for the determination of blood concentration: total solids by dry weight, which requires the loss of considerable blood; estimation of hemoglobin by various methods, which cannot be corrected for reduction of hemoglobin without reduction of red corpuscles (Korth and Marx, 1928); determination of total solids with the haematokrit, which fails to record changes in size of corpuscles with various tensions of CO_2 (Smirk, 1928); specific gravity of the blood, an indirect method; the refractometric determination of total proteins; and the increase in the number of erythrocytes. In the present experiments, the latter method was used because the red blood corpuscles are the most stable elements of the blood under the conditions of the experiment. Blood samples were taken from the saphenous vein, without anesthesia, to avoid the concentration of corpuscles in the capillaries of the skin which Uthelm (1920) has shown may occur in dehydration.

The effects of dehydration on the blood concentration of adult cats deprived of all water except that contained in cooked, lean meat, as indicated by red corpuscle counts at 72-hour intervals, are shown in Figure 2. A rather wide variation in the normal number of red corpuscles per cubic millimeter of blood may be noted. Two factors may have influenced this: age of the individual and the effect of emotion on the contraction of the spleen. Czerny (1894) gave an average of 7,372,444 corpuscles per cubic millimeter for 3 young cats of 355-416 gm. in weight. Wells and Sutton (1915) found an average of 9,646,000 corpuscles per cubic millimeter of blood in the cat, but made determinations on only 2 animals. The average normal count for the 16 cats reported here was 8,922,500 red corpuscles per cubic millimeter. Powers, Bowie, and Howard (1930) made red-corpuscle counts on 25 normal, male dogs and found an average of 7,002,000 corpuscles per cubic millimeter, with variations of from 5,070,000 to 8,610,000 per cubic millimeter, which variations are in accord with variations found in the 16 cats herein reported.

Since Barcroft and Barcroft (1923) established that the spleen functions as a reservoir for the red corpuscles, many workers have shown that various physiological states may result in a contraction of the spleen and an increase in the number of red corpuscles present in the circulating blood. More recently, several investigators have reported contraction of the spleen under conditions of excitement or

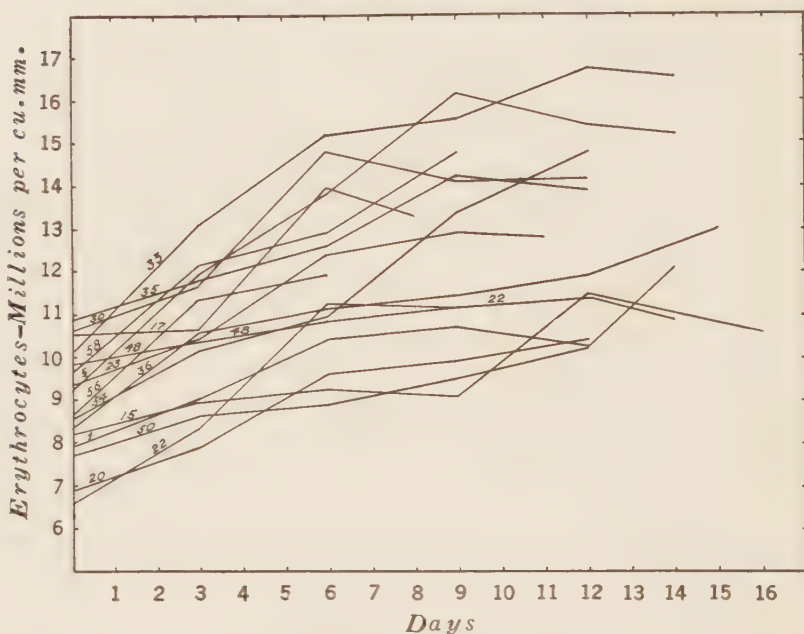


FIG. 2.—Blood concentration from dehydration. The first points on the left indicate the number of erythrocytes prior to dehydration. The number of each experiment is shown by figures on the curves; the duration of dehydration is given in days.

emotion. In a study on man, Benhamou, Marchioni, and Nouchy (1929) found an increase of 9 per cent in the number of red corpuscles present in the circulating blood when an unexpected explosion was used as the exciting agent. Barcroft (1930), after a careful study of the effect of emotion on the spleen of the dog, reported a reduction of 50 per cent in the size of the exteriorized spleen of a dog when it heard a cat mew in an adjacent room. It is difficult to make a fair comparison with animals which do not have the same ratios between spleen weight and body weight. The spleen of the cat represents

0.05 per cent of body weight, while that of the dog and man represent 0.25 per cent of body weight (Krumbhaar, 1926). Field (1930) found a decided increase in the platelet count of cats when excited from being tied to a board for 3 minutes. In the cat, Cruickshank (1926) found that the blood expelled from the spleen may have 20-40 per cent greater content of hemoglobin than the blood in the general circulation, and that the amount which could be added

TABLE IV

CHANGES IN BLOOD CONCENTRATION IN RELATION TO DURATION OF DEHYDRATION,
RATIO OF WATER INTAKE TO OUTPUT, AND NEGATIVE WATER
BALANCE IN PERCENTAGE OF ORIGINAL BODY WEIGHT

Cat. No.	Original Weight (Grams)	Duration of Dehydration (Days)	Ratio of Water Intake to Output	Negative Water Balance in Percentage of Original Weight	Blood Con- centration on Last Day in Percent- age Increase
1.....	2,837.0	13.5	1:2.30	28.4	52.58
5.....	3,080.5	14.0	1:2.90	30.9	65.36
15.....	1,225.0	16.0	1:1.40	25.1	28.03
17.....	2,181.0	7.5	1:3.09	22.7	26.42
20.....	1,943.5	11.5	1:3.47	32.9	50.86
22.....	3,294.0	13.5	1:3.46	26.3	63.48
23.....	1,393.5	11.0	1:3.31	33.9	38.67
30.....	2,737.5	12.0	1:2.00	20.9	34.12
33.....	3,298.5	14.0	1:2.65	24.2	63.73
35.....	2,396.0	12.0	1:2.83	31.6	28.49
36.....	2,730.5	15.0	1:3.33	28.3	56.73
48.....	2,323.0	9.0	1:10.1	16.6	14.28
50.....	1,949.5	12.0	1:3.51	29.0	33.93
54.....	2,266.0	12.0	1:4.66	30.1	72.13
56.....	1,791.5	6.0	1:18.1	20.2	37.50
58.....	2,331.5	9.0	1:9.39	19.3	53.31

to the circulation was 2.6-5.6 per cent of the total blood volume. From these figures it may be estimated that the maximum increase in the hemoglobin of the circulating blood following splenic contraction would be less than 2.5 per cent. The cats used in these experiments were not tied when blood samples were drawn, but in many cases the animals were held with considerable force and undoubtedly did experience considerable emotional excitement. From the literature available on this subject it seems probable that an error of 5 per cent may have been introduced into the blood counts through splenic contraction. In view of the high concentrations encountered, this would not materially affect the results. Table IV shows definite

relations between blood concentration, water intake and output ratios, and negative water balance in percentage of body weight.

The percentage of increase in blood concentration on the last day of the experiment is, in half of the experiments, not the greatest concentration attained. There was often a reduction in concentration near the end of the experiment, especially in the longer experiments. This reduction may have been the result of a failure on the part of the body to replace corpuscles, due to nutritional disturbances. Marriott (1923) reported a decrease in the concentration of hemoglobin and of serum protein after a number of days of severe anhydremia. In a study of the effects of reduced blood volume on tissue maintenance, Rous and Gilding (1929) reported that, after hemorrhage in cats and rabbits, the red bone marrow was well served with blood although situated in limbs almost deprived of a circulation. To some extent starvation may have affected the replacement of red blood corpuscles, although Robertson (1913) reported that in the fasting dog and rat the percentage of hemoglobin and the number of blood corpuscles were not appreciably affected.

White blood corpuscle counts were made throughout the experiments; but, other than a general increase in number with dehydration, there were no significant changes.

RESPIRATORY EXCHANGE DURING DEHYDRATION

The literature relative to the effect of dehydration on gaseous metabolism is very limited. Straub (1899) reported no change in carbon-dioxide production of one dog deprived of water and fed air-dried meat powder for 3 days. Warburg (1909) and Loeb and Wasteneys (1913) reported an increased rate of oxidation in unfertilized sea-urchin eggs when placed in hypertonic solutions. Caldwell (1925) reported increased carbon-dioxide production in several species of animals, including the frog, after dehydration in dry air. Iizuka (1926) desiccated frogs in several ways and at different temperatures and found an increase of more than 55 per cent in carbon-dioxide production following desiccation over sulphuric acid for 24 hours. The increase in oxygen consumption was less, which resulted in an increased respiratory quotient.

When these experiments were undertaken, the question of dehy-

dration in relation to maintenance of body temperature was in a highly unsatisfactory state. Therefore, no attempt was made to measure the respiratory exchanges until seven of these experiments and several preliminary ones indicated that, under the conditions of the experiment, dehydration did not affect body temperature. Air samples were drawn usually 12 hours after feeding, but in some cases less time had elapsed. The samples probably did not always represent post-absorption metabolism, but the increase in metabolism due to digestion must have been small. Sonderstrom, Barr, and DuBois (1918) showed that a small standard breakfast increased the basal metabolism of three men only 7 per cent for the first hour and not at all after 6 hours. Since it is impossible to estimate the degree of relaxation under such circumstances, no claim is made that the metabolism of the experimental animals was at a basal rate; but the standard procedure followed justifies a comparison of control and experimental results. The carbon-dioxide production and oxygen-consumption data were reduced to 0°C ., 760 mm. Hg., dry, with corrections for brass scale barometer.

Loewy (1911) found the oxygen consumption of normal cats to be 1.005 gm. per kilogram hour and the carbon-dioxide production to be 1.064 gm. per kilogram hour. The averages for the cats in these experiments are: oxygen consumption 0.892 gm. and carbon-dioxide production 0.899 gm. per kilogram hour. The normal averages are lower than Loewy's figures, but higher than those of Aub, Foreman, and Bright (1922), who used cats in a study of the effect of adrenal-ectomy on metabolism. These workers made a large number of determinations on 9 normal cats and selected the lowest results as control rates. Their cats also exceeded the average weight of the cats in this report by 34 per cent, which, according to the Law of Surface Area, would result in lower rates when calculated on the basis of body weight. Heat production in calories per square meter of surface were not calculated in these experiments, because the constant used in such calculations was determined on normal cats and because, after a few days of desiccation, the normal weight-surface relations would be in error.

The greatest increases in respiratory exchange were noted between the second and the seventh day of dehydration (Figs. 3 and 4).

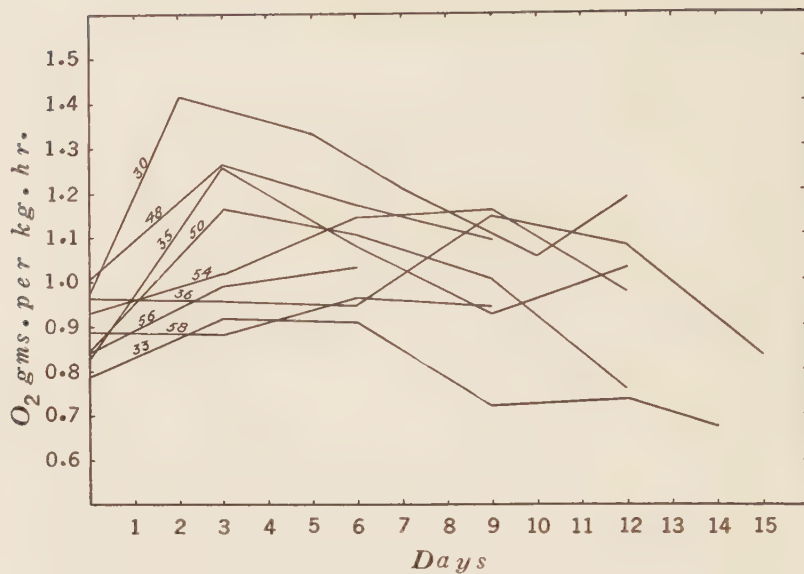


FIG. 3.—The normal oxygen consumption of the cats and the increase or decrease during dehydration. The number of each experiment is shown by figures on the curves; the duration of dehydration is given in days.

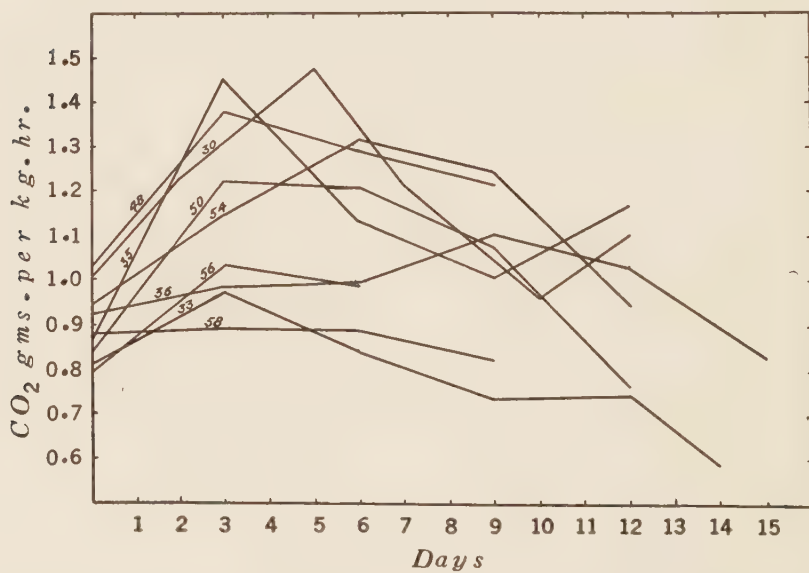


FIG. 4.—The normal carbon-dioxide production of the cats and the increase or decrease during dehydration. Figures on the curves indicate the number of the experiment; the duration of dehydration is given in days.

After the seventh day, there was a gradual decrease, and in experiments extending longer than 9 days an average rate considerably below normal. The greatest increases in oxygen consumption averaged 28.8 per cent. The average increase for all of the experiments and for the entire period of dehydration was 14.9 per cent. The increase in carbon dioxide production was greater than in oxygen consumption. The greatest increases in carbon-dioxide production averaged 33.9 per cent, and the average increase for the duration of dehydration was 18.3 per cent. In the frog (Caldwell, 1925, and Iizuka, 1926), the increase in carbon dioxide was much greater, but the frog gives up its water very quickly when exposed to circulating dry air. There is some evidence that an increase in respiratory exchange occurs before the animal has lost sufficient water to dehydrate the tissues to an appreciable extent. This suggests the possibility that respiratory metabolism is stimulated by the increased rate of evaporation from the mucous membranes in dry air.

Loewy (1911) found the respiratory quotient of normal cats to be 0.77; and Aub, Foreman, and Bright (1922) reported an average respiratory quotient of about 0.78, with variations from 0.73 to 0.96. The normal respiratory quotient of these cats varied from 0.70 to 0.79, and averaged 0.74. Dehydration had no marked effect on the respiratory quotient. With one exception, the respiratory quotient increased slightly for the first 3 days of dehydration (Fig. 5). This may have been the result of increased blood flow to the mucous membranes to supply moisture lost from contact with dry air, which would result in greater ventilation of the blood. The decrease in respiratory quotient characteristic of a fasting condition (Benedict, 1915) did not appear in these experiments.

METABOLIC-WATER PRODUCTION

Water formed in the metabolic processes of the body may be considered, according to its source, as intramolecular water, water of oxidation, and water of syntheses. The term "metabolic water" generally refers to the total water produced from all three sources. Intramolecular water may be liberated from oxidized organic material supplied as food or from organic material synthesized in the body. In the second event the oxygen which united with hydrogen

to form water would be an addition to the body weight as a result of respiration. In the production of water of oxidation all of the oxygen which united with hydrogen to form water would result in an increase in body weight.

Water production as a result of metabolism has been recognized since the early work in chemical physiology; and estimates for man, based on computations of the amount of hydrogen oxidized, vary from 150 to 400 gm. per day. Babcock (1912) pointed out that the

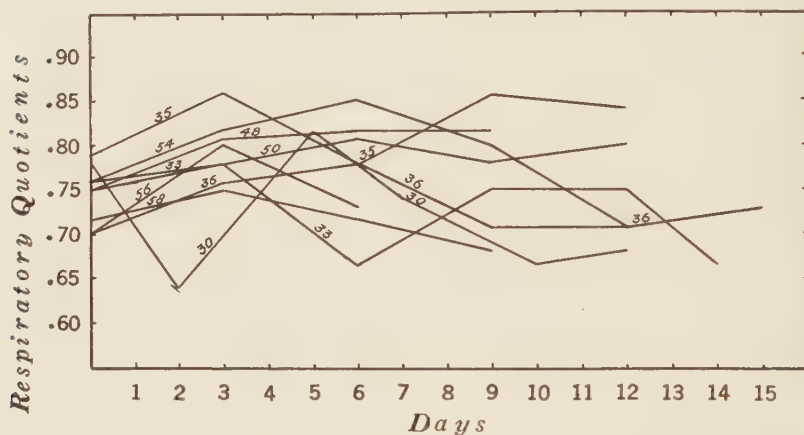


FIG. 5.—The normal respiratory quotients of the cats and the effect of dehydration on the respiratory quotient. Figures on the curves indicate the number of the experiment; the period of dehydration is given in days.

same carbon nucleus may function several times in hydrolytic and dehydrating reactions, and suggested that metabolic water has a function which cannot be served by imbibed water. Since metabolic water is produced within the cell, it reduces the concentration of the cell contents and thereby disturbs the osmotic equilibrium between the fluids without and within the cell, with the result that nutrients move to the region of lower concentration; while imbibed water causes reduction of concentration on the outside of the cell which aids elimination from the cell but hinders the movement of nutrients into the cell. Babcock has also shown that metabolic-water production is of particular importance to animals living on air-dried food, such as the clothes moth, pea weevil, and other insects which do not have access to free water.

An attempt has been made in these experiments to determine the quantity of metabolic water produced by cats while undergoing a slow but severe dehydration. Protein yields less metabolic water than other foodstuffs, i.e., 41 per cent as compared to 55 per cent in carbohydrates, and 110 per cent in fat metabolism. For this reason, a diet high in protein content, made up only of lean meat from which all visible fat had been removed, was given the animals for several weeks prior to and throughout the experiment. This, obviously, does not mean that fat and glucose in addition to that present at the beginning of the experiment is not oxidized; but fats and glucose formed by syntheses, when oxidized, give up the intramolecular water acquired in the process of synthesis as water of metabolism.

The metabolic water produced in these experiments was first calculated from the total intake and output of water, assuming that the total loss in weight of the cat was water and making a correction of these figures for carbon loss in carbon-dioxide excretion and for the additions to the weight of the cat in the form of dry weight of the food. It was then found that precisely the same results were obtained from calculations based on the total intake and output of the cat in relation to its initial and final weights. This gave the addition to the weight of the cat in oxygen absorbed but not excreted as carbon dioxide. Since the hydrogen utilized in the production of metabolic water was already present, the actual weight of the water so formed would be 1.1118 times that of the oxygen utilized. As the latter method is less complicated and all experiments have been calculated by both methods with identical results, only the latter method will be presented in detail. All totals for the determinations as given below were taken from the data on experiment No. 36. On account of the large volume of data, it is only possible to present results in brief form.

INTAKE

250.59 gm. dry weight of food

331.91 gm. water in food

582.50 gm. total ingesta

OUTPUT

471.00 gm. urine

616.00 gm. water collected in desiccator

19.53 gm. water in feces
18.67 gm. solids in feces
234.48 gm. carbon excreted as carbon dioxide
1359.68 gm. total egesta
2730.50 gm. original weight of cat
582.50 gm. total ingesta
3313.00 gm. original weight of cat+total ingesta
1359.68 gm. total egesta
1953.32 gm. weight of cat if no water had been formed
2140.50 gm. actual final weight of cat
1953.32 gm. final weight if no water had been formed
187.18 gm. addition to weight of cat from oxygen utilized in metabolic-water production
187.18 × 1.1118 = 208.10 gm. metabolic water produced

An estimate of the calorie production, based on an average caloric value of a liter of oxygen as calculated from the tables of Benedict and Fox (1925), showed that the total calorie production in each experiment was at least 20 per cent greater, with the exception of experiment No. 15, than the possible calorie production from the food consumed by the animal. Since the animals, therefore, must have metabolized some of their own tissues, it seems reasonable to assume that none of the oxygen retained under the conditions of the experiment was utilized in tissue production. Solids in the urine do not affect the total of metabolic water produced, when calculated on the basis of entire intake and output. The metabolic water in grams per kilogram day was calculated from the average weight of the cat, determined from the morning and evening weights.

Table V shows the metabolic-water production for each experiment in relation to loss of weight, water intake-output ratios, and duration of the experiment for both the entire period and for each half. These results give only the minimum metabolic-water production and do not take into consideration intramolecular water from nutrients not synthesized in the animal. Some water was undoubtedly lost in collection of urine from the pans; and all water from respiration was lost while the animals were out of the respiratory

TABLE V

METABOLIC-WATER PRODUCTION IN RELATION TO BODY WEIGHT, RATIO
OF WATER INTAKE AND OUTPUT, AND DURATION OF DEHYDRATION

CAT No.	ENTIRE PERIOD OF DEHYDRATION					FIRST AND LAST HALF DEHY- DRATION PERIODS		
	Initial Weight (Grams)	Loss in Weight (Grams)	Duration of Dehy- dration (Days)	Ratio of Water Intake to Output	Metabolic Water Produced (Grams per Kilogram Day)	Duration of Dehy- dration (Days)	Ratio of Water Intake to Output	Metabolic Water Produced (Grams per Kilogram Day)
1....	2,837.0	549.5	13.5	1:2.30	4.67	{6.5 7.0	1:2.27 1:2.34	6.32 3.04
5....	3,080.5	682.0	14.0	1:2.90	4.93	{7.0 7.0	1:3.07 1:2.65	4.15 5.82
15....	1,225.0	3.5	16.0	1:1.40	4.65	{8.0 8.0	1:1.17 1:1.88	6.04 3.25
17....	2,181.0	390.0	7.5	1:3.09	6.73	{3.5 4.0	1:2.18 1:6.60	5.75 7.69
20....	1,943.5	463.5	11.5	1:3.47	4.52	{5.5 6.0	1:4.80 1:2.76	5.18 3.86
22....	3,294.0	666.0	13.5	1:3.46	5.66	{6.5 7.0	1:3.50 1:3.39	4.81 6.57
23....	1,393.5	340.5	11.0	1:3.31	6.11	{5.5 5.5	1:3.65 1:2.92	5.30 7.03
30....	2,737.5	353.5	12.0	1:2.00	6.33	{6.0 6.0	1:1.60 1:2.94	6.36 6.29
33....	3,298.5	537.0	14.0	1:2.65	4.01	{7.0 7.0	1:2.47 1:3.07	4.24 3.71
35....	2,396.0	514.5	12.0	1:2.83	6.31	{6.0 6.0	1:2.45 1:3.96	7.25 5.23
36....	2,730.5	590.0	15.0	1:3.33	5.65	{7.5 7.5	1:2.83 1:4.46	6.16 5.08
48....	2,323.0	368.5	9.0	1:10.1	8.07	{4.5 4.5	1:7.02 1:23.0	7.90 8.25
50....	1,949.5	429.5	12.0	1:3.51	5.31	{6.0 6.0	1:3.72 1:3.29	4.60 6.11
54....	2,266.0	579.0	12.0	1:4.66	7.11	{6.0 6.0	1:3.30 1:15.9	6.45 7.85
56....	1,791.5	343.0	6.0	1:18.1	8.46	{3.0 3.0	1:12.4 1:84.4	8.73 8.16
58....	2,331.5	418.0	9.0	1:9.39	6.60	{4.5 4.5	1:5.73 1:174.0	5.66 7.63

chamber, approximately 2 hours each day. These losses would have increased the total output from the animal and thereby increased the calculated metabolic water produced to the same extent. The carbon loss would have been more accurate had it been possible to make continuous carbon-dioxide-production determinations. For the experiments in which gaseous exchange was not determined, the carbon loss was estimated on the basis of the average per kilogram hour for the experiments in which carbon-dioxide production was determined.

No literature has been found on metabolic-water production in animals lower than man; therefore it is difficult to make comparisons. Rogers (1928) estimated, on the basis of diet, a metabolic-water production in man of 300-400 gm. per 24 hours. For a 75-kg. man this would average from 4 to 5.3 gm. per kilogram day. The average for the 16 cats in these experiments was 5.94 gm. per kilogram day. Benedict and Carpenter (1910) made a large number of determinations on the metabolism of healthy man during rest and found an oxygen consumption of approximately 0.367 gm. per kilogram hour. The average normal oxygen consumption of the cats in these experiments was 0.892 gm. per kilogram hour, or a rate 2.4 times as great as that in man. Since metabolic-water production is dependent, in part, upon rate of oxidation, if the estimates on metabolic-water production in man are correct, the cats should have produced from 9.6 to 12.7 gm. of metabolic water per kilogram day, or almost twice the average minimum quantity measured in these experiments. This would have been possible had a mixed diet been used and the intramolecular water included.

DISCUSSION

Because of the importance of water in all of the vital processes of animals, the physiological responses to a disturbance of water balance are undoubtedly numerous and of far-reaching consequences. Experiments of various kinds have shown that water is more vital than food but less vital than oxygen. Many physiological effects from a derangement of the equilibrium of water metabolism could probably be referred to histological changes in certain organs and tissues of the body if sufficient data were available for correlation.

Garofeanu and Derevici (1924) studied the histological changes in the tissues of dogs deprived of water from 4 to 9 days, and reported lesions in the tissues of many organs even from the first day. The lungs, the liver, and the thyroid suffered to the greatest extent from water deficiency; but lesions appeared in the intestinal mucosa, adrenals, kidneys, and all other glandular tissues studied. The latter is in accord with the results of Kudo (1921*b*), who found the greatest proportional losses in weight in the glandular structures of the body when rats were deprived of water. Since many physiological reactions are subject to modifications through hormone action, it would be expected that changes would occur with stimulation or depression of the activity of the endocrine glands from dehydration. Sufficient knowledge is not available on the effects of water losses to predict either hyperactivity or hypoactivity following lesions from water deficiency. Since the thyroids control, to a considerable extent, the respiratory metabolism of animals, it is not inconceivable that the increase in gaseous metabolism found in dehydrated cats may have resulted from stimulation of the thyroids due to lesions produced by water losses; however, there is no experimental evidence that this was even a contributory factor. Hammett (1927) ascribed the anhydremia which accompanies thyroid and parathyroid deficiency to lowered nutritional level rather than to any specific relation of the glands to water balance. There is considerable evidence that the posterior lobe of the hypophysis functions in the maintenance of normal water balance, but the mechanism is unknown. Priestley (1921) determined that the diuresis induced by water-drinking could be delayed for 4-6 hours by injections of pituitrin. The diuresis is then accompanied by an increased excretion of chlorides. Weir, Larson, and Roundtree (1922) have shown from experiments on dogs that the antidiuretic effect of pituitary extract is independent of the nerve supply of the kidney. Polydypsia and polyuria are recognized symptoms of diabetes *insipidus* and are related to deranged water metabolism. Roundtree has reported urinary outputs from diabetes *insipidus* cases in excess of 14 liter per day, which could be temporarily reduced by extracts of the posterior lobe of the hypophysis. Adolph and Ericson (1927) showed that the kidney of man is insensitive to an excess of water in the blood when pituitrin is

administered. Downs and Geiling (1929) showed that mice which received alkaline extracts of the anterior lobe of the pituitary gained weight more rapidly than controls but that their tissues contained from 6 to 8 per cent more water than the tissues of controls. Some work indicates that the hypophysis is only of minor importance in water-balance equilibrium. Camus and Roussy (1920) removed the hypophysis from dogs and reported only a transitory polyuria following the operation. More than a month later, when the animals had recovered from the first polyuria, a second polyuria was produced by puncture of the tuber cinereum. Bailey and Bremer (1921), Rogers (1924*b*), Kayser (1929), and others have produced polyuria and blood concentration by lesions of various parts of the midbrain without injury to the hypophysis; however, this does not eliminate the possibility that injury to nerve tracts connecting with the hypophysis may have been the immediate cause. Molitor and Pick (1925) and Hoffman and Wertheimer (1927) have suggested a central nervous control of water balance in the midbrain, but conclusive proof is not presented. Liu and Krüger (1927) reported a polyuria and hydremia after midbrain puncture and concluded that certain midbrain regions not only controlled kidney function but influenced vascular permeability and tonus.

Kudo (1921*a*) reported no loss in weight of the brain and spinal cord in rats deprived of water; but in a study of the effects of withdrawal of water on the salivary conditioned reflex induced by morphine, Crisler (1928) found that conditioned secretion of saliva in the dog was practically abolished after 3 to 5 days of dehydration. This worker reported that the peripheral mechanism was little affected, and concluded that dehydration resulted in a depression of certain central processes. The dehydrated cats reported here showed a marked change in behavior which suggests a depression of sensory centers; this fact is difficult to understand, when accompanied by an increase in respiratory exchange, unless dehydration of peripheral nerves increased muscular tonus.

In the dehydration of body tissues the movement of water from the intercellular and intracellular spaces to the blood vessels must take place against the hydrostatic pressure within the capillaries. The colloid osmotic pressure of the plasma proteins must play an

important rôle in this absorption process. Landis (1928) measured the pressure in the arteriolar end and venous end of the capillaries of the mesentery of rats and guinea pigs and found an average arteriolar pressure of from 30 to 40 cm. of water and an average venous pressure of 11.5 cm. of water. The osmotic pressure of the plasma proteins was 22–27.5 cm. of water. Under these circumstances, filtration of water would take place at the arteriolar end and absorption at the venous end. With a reduced volume of blood, as in dehydration, the filtration pressure would decrease while the increased concentration of the blood would result in a higher osmotic pressure of the colloids and a greater movement of water into the blood stream. Inanition from starvation would accentuate the concentration of blood through a decrease in plasma proteins but would tend to lower the dehydration rate of the tissues. For this reason, the results of experiments on starved animals deprived of water are hardly comparable to experiments on animals deprived of water with food *ad libitum*.

Clinical evidence of disturbance of water balance associated with the symptom fever has been noted so widely that a review of the literature at this time would be superfluous. The effect of disturbance of water balance on body temperature has received much less attention, although pediatricians have long recognized the clinical significance of acute water loss in inanition fevers and retention toxicosis in infants. Schiff (1929) points out that uncomplicated pictures of water deficiency are rarely seen on the sick bed. By controlling the diet, Schiff and his co-workers have reduced the water intake of a large number of children to about 40–50 per cent of the normal needs, and report an increase in body temperature in half of the cases, with wide individual differences in symptom complexes. If reduction of free water by an increased capacity for fixation by the colloids is responsible for the symptom fever, as proposed by Balcar, Sansum, and Woodyatt (1919), the animals in these experiments should have demonstrated a hyperthermia at some stage of dehydration, since, while not so rapid, the reduction of free water was greater. Andrews (1926) concluded from his experiments on dogs that a low-grade fever is always present in dehydrated animals. These results fail to confirm such a conclusion.

While these experiments have been an attempt to study some phases of water metabolism in a laboratory animal under severe conditions, the results may have some significance in the water relations of desert animals, which must encounter even more severe conditions in their normal environments.

The facts that the only cat of this series which was fed uncooked beef consistently gained in weight with a reduced water intake and that dehydrated cats which had refused cooked meat for several days would eat raw meat may indicate that carnivorous animals in an arid region are quite independent of free water for long periods. However, the herbivorous animals of desert and semidesert regions, some of which feed largely on air-dried seeds and grasses and will not drink when water is available (Bailey, 1923), have no comparable source of water. Metabolic water furnishes a constant supply, which may be augmented by increased respiratory metabolism when obligatory water has been reduced to a minimum; but the amount of metabolic water produced is directly dependent upon the free hydrogen available from oxidation of food or tissues of its own body, and therefore the quantity is necessarily limited.

No physicochemical mechanism for water conservation such as that which occurs in birds and scaly reptiles in the excretion of uric acid crystals has been described for mammals. Whether the maintenance of normal water balance is regulated through the nervous system, through hormone action, through physicochemical changes, or a combination of these cannot at present be predicted; but the adaptation of certain mammals to the reduced water intake of desert conditions must involve important physiological changes in organs which have to do with nutrition and elimination; the investigation of these not only should add materially to the scanty knowledge of the physiology of desert animals but should contribute to the general physiology of water metabolism, which in turn is fundamental to a proper understanding and solution of one of the most important problems of the ecology of desert animals.

SUMMARY

1. Adult cats have been dehydrated by water deprivation in dry air, without acute starvation, to such an extent that the

negative water balance averaged 26.8 per cent of the original body weight.

2. The average increase in blood concentration which resulted from dehydration was in excess of 45 per cent of the original blood volume. An increase of 75 per cent was recorded without fatal results.

3. The maintenance of normal body temperature was not affected by dehydration from water deprivation. There was no indication that a reduction of free water results in an increase in body temperature.

4. Metabolic-water production was not noticeably increased with increasing severity of dehydration. There was some evidence that cats could live for long periods on a diet of flesh and blood, such a diet as might be obtained from a recently killed animal.

5. Dehydration increased the total respiratory exchange of the cats without marked effect on the respiratory quotient. There was a decided decrease in respiratory exchange before the vital limit of dehydration was reached.

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